

REMARKS

Applicant thanks the Examiner for the courteous telephone interview granted applicant's representative, Dr. Paul Fenster, on December 13, 2006. The following discussion *inter alia* summarizes the arguments made by the undersigned regarding the cited art and its relevance to the claims.

The application includes claims 1, 2, 5, 7 - 11, 13 - 17, and 19 - 32. Claims 3, 4, 6, 12, and 18 are cancelled; claims 23 - 32 are new; and claims 1, 2, 5, 7 - 11, and 13-16 are currently amended.

Claims 1-5, 7, 10-11, 13, 16-17, and 19-22 were rejected under section 102 and claims 6, 8, 12, 14, 18, and 20 were rejected under section 103, all in view of Fuhrman et al.

In the amendments, claims that had to do solely with LDL susceptibility to retention and aggregation were deleted, and claims that had to do with cholesterol levels were separated from the other claims, for ease of discussion.

The claims are now limited to relate only to treating risk-factors or conditions that are far from being obvious in view of Fuhrman et al.

At the outset, if Applicant accepts, for the sake of the argument, that the licorice extract mentioned in the claims is not patentably distinct from the extract mentioned by Fuhrman et al, all that has to be discussed is whether treating the risk factors or conditions recited in the claims is obvious (or anticipated) in view of the disclosure of Fuhrman et al.

Fuhrman et al. described that the licorice extract reduced LDL susceptibility to oxidation, and reduced atherosclerotic lesion in atherosclerotic mice. *As to application to the claimed risk factors it was either silent or taught against.* For example, Furman's data shows that various lipid levels in the blood were substantially unaffected by the extract. There was no reason to believe, based on the paper, that this would be any different for patients with the risk factors claimed.

The claims as amended do not claim treating atherosclerosis, neither reducing LDL susceptibility to oxidation.

Not only is Furman silent about or teaches away from treating the risk factors with licorice extract, a person of skill in the art would not have expected that the extract would alleviate the other risk factors. The claimed risk factors and conditions are conventionally treated with medicaments different than those used to treat atherosclerosis. For instance, blood pressure is treated with one drug, and atherosclerosis with another. If a patient suffers from both, the patient is generally

administered two different medications, one for each condition. Similarly, high cholesterol is conventionally treated with Statins which are unrelated to licorice extract. There would be no reasonable expectation of success in such treatment. Applicant submits that it would not even rise to the level of "obvious to try" which itself is not enough to provide a *prima facie* case of obviousness, let alone anticipation. It is therefore not obvious, and certainly not inherent, to treat any of the claimed risk-factors or conditions with Fuhrman's licorice extract.

The Examiner argued that "the patient of the claims is not even required to be suffering from a risk factor or be susceptible to a risk factor". Applicant respectfully submits that the claims do relate to treating a patient "suffering from said risk factor" (see claim 1). Similar language is used in claims 7, 8, 9, and 10. Additionally, the claims were amended to include a step of identification that the patient suffers from the risk factor or condition.

Applicant respectfully submits that the Examiner's statement that "the lowering of the risk factors as claimed would be the result of administering the licorice extract of Fuhrman" is made in hindsight. Fuhrman did not administer the extract to people in need, and does not provide any reason to believe that had the extract been given to people in need, it would be beneficial for relief of the claimed risk factors. As indicated above, the medications used for treating atherosclerosis and for treating the claimed conditions are different.

The Examiner states that "Fuhrman et al. is the documentary evidence along with Applicant's second noted document of record which teaches that antioxidants lower risk factors". However, Applicant respectfully submits that not every risk-factor is lowered by every antioxidant, and the claims are only for lowering certain risk factors with a very specific anti-oxidant. Thus the examiner's statement explains, at most, why was the Applicant motivated *to try* treating the claimed risk factors or conditions with Fuhrman's licorice extract.

In the following, each risk-factor or condition is related to briefly:

1. Blood pressure or hypertension (claims 2, 28).

Hypertension is known as a factor that increases the risk for atherosclerosis. Therefore, reducing blood pressure may be helpful in preventing or alleviating atherosclerosis. The teachings of Fuhrman et al. could be considered obvious in view of teachings of the present application, but not vice versa. The fact that the end-result (atherosclerosis) may be treated by the licorice extract does not teach or render obvious the finding that the cause (hypertension) may also be treated with the same agent.

Patients that suffer from both atherosclerosis and hypertension are usually treated with two different agents, each to treat one of the conditions. Even if there are some medicaments that treat both conditions, it is not at all obvious that Fuhrma's licorice extract is one of them.

Furthermore, patients that suffer from atherosclerosis not necessarily suffer from hypertension. To support this statement, Applicant submits a copy of an article named "Endothelium-mediated Coronary Blood Flow Modulation in Humans", published at J. Clin. Invest. 92 (August 1993) pages 652-662. The article describes a group of 12 people "with evidence of early atherosclerosis but normal cholesterol levels and normal blood pressure" (see abstract) [emphasis added]. Therefore, treating with the licorice extract people that suffer from atherosclerosis is inherently different from treating with the same extract people that suffer from hypertension.

Finally, the licorice extract is not known to include any constituent which is known in the art to be effective against hypertension, therefore, a skilled person would not expect the extract to have the claimed efficacy.

2. Lowering total cholesterol levels (claim 23, 31) and LDL levels (claim 24).

Reducing the susceptibility of LDL to oxidation, which is described by Fuhrman et al is expected to result in having less oxidized LDL. Since oxidized LDL is not found in the blood, but rather sticks to the blood-vessel walls, reducing LDL oxidation could result in leaving *more* LDL in the blood, and thus, increasing, rather than decreasing, its blood concentration. Thus, Fuhrman teaches away from trying to treat these conditions with the licorice extract.

Furthermore, Fuhrman itself teaches that administering the licorice extract to humans resulted in no significant change in cholesterol, it was only the inventor, who surprisingly found that against what would be expected in view of Fuhrman, cholesterol *is* lowered in hypercholesterolemic patients. In fact, this was non-obvious enough, so that Fuhrman herself published, in 2002, another research, titled "Antiatherosclerotic Effects of Licorice Extract Supplementation on Hypercholesterolemic Patients: Increased Resistance of LDL to Atherogenic Modifications, Reduced Plasma Lipid Levels, and Decreased Systolic Blood Pressure". A copy of this publication, published in Nutrition, 18 (2002) 268-273 is attached herewith.

There is no reason to believe that an agent effective in reducing the susceptibility of LDL to oxidation will be also effective in reducing LDL levels or total cholesterol levels. The above mentioned article teaches that the 12 atherosclerotic people had normal cholesterol levels, thus, treating cholesterol levels is inherently different from treating atherosclerosis.

3. Lowering LDL levels and triglyceride levels (claim 26, 30-32) without decreasing HDL level (claim 8).

Applicants fail to understand how the disclosure of Fuhrman renders any of these effects obvious, and fail to find an explanation in the Office Action. If claim 8 remains rejected, or any of new claims 23-32 is rejected, clarification of the basis for the rejection is kindly requested.

4. Lowering glucose concentration in the blood (claim 5), treating chronic renal failure (claim 29).

Applicant fails to understand how the disclosure of Fuhrman renders claim 5 (or new claim 29) obvious, and fails to find an explanation in the Office Action. If claim 5 remains rejected or new claim 29 is being rejected, clarification of the basis for the rejection is kindly requested.

Finally, Applicant is going to file in the following days an affidavit signed by an author of Fuhrman et al, substantiating factual findings mentioned above.

Respectfully submitted,

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